REMARKS

Reconsideration of the rejections set forth in the Office action mailed September 23, 2003 is respectfully requested. Claims 13-17, 21, and 24-29 are currently under consideration; claims 18-21 have been withdrawn. No amendments are made with this response.

I. Specification

The Examiner continues to assert that the articles and non-US patent publications referred to on page 10, lines 20-29 of the specification disclose "essential material", and that these publications "provide enabling disclosure of how to make the peptoids".

In the previous Office Action, the Examiner stated that the applicant should "amend the disclosure to include the material incorporated by reference." It is not clear whether this is meant to include only the PCT publication given as an example ("e.g., WO 98/06437") or all of the publications listed at page 10, lines 20-29, which total nineteen in all.

Per the remarks below, the applicants can find no compelling reason under the US patent laws and regulations to insert the text of the above-referenced PCT publication, much less the text of nineteen publications, into the specification.

With respect to "enabling disclosure of how to make the peptoids", the purpose of the enablement provision is to assure that the inventor provides sufficient information about the claimed invention to allow a person of skill in the field of the invention to make and use it without undue experimentation, relying on the patent specification and the knowledge in the art. *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 1001 1006 (Fed. Cir. 1991). The Examiner has provided no evidence that the existing disclosure does not meet this standard with respect to the claimed method of identifying peptoids. (Applicants note, in this respect, that the Examiner's two references to the "claimed peptoids", on page 3 of Office Action, are misplaced. The claims are directed to a method, not to a peptoid.)

Further, the specification incorporates by reference a US patent and several US applications, which may be used to incorporate "essential" material (MPEP 608.01(p)), and which describe the preparation of peptoids. These include U.S. Patent No. 5,877,278 (at the location noted above) and US applications 60/023,867, 60/054,743, 07/950,853, and 09/132,808 (page 15, lines 30-31).

(Applicants also note that the "foreign references" (PCT publications) cited at page 10, lines 20-29 are based on these US applications; see page 15, lines 30-31.)

In addition, peptoid synthesis is briefly described on page 15, and a working example describing peptoid synthesis is provided (pages 22-23).

Even if further description of peptoid synthesis, beyond that literally provided in the specification, were considered "essential", the Examiner has provided no evidence that the disclosure of the above-referenced US patents and applications is not sufficient for this purpose.

II. Rejections under 35 U.S.C. §112, First Paragraph

Claims 13 and 21 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the invention was filed, had possession of the claimed invention.

The Examiner first referred to step (iii) of claim 13: "screening each cell for transfection of the oligonucleotide, to identify transfected cells". In the previous response, the applicants pointed to page 11, lines 9-10 for support of this language. This was apparently a typographical error on the part of the applicants. Support is in fact found in the paragraph bridging pages 18-19 of the specification, as follows:

> The *cells are then screened for transfection of the oligonucleotide*, according to methods known in the art. One such method comprises detecting a label, such as FITC, on the oligonucleotide. *Cells that have taken up the oligonucleotide/peptoid complex can be identified*, after washing, by scanning for FITC fluorescence using a fluorescent plate reader.

For support of the phrase "each said mixture is contacted with a plurality of distinct cell types" in claim 21, the applicants pointed to the description in the specification of two screening experiments, each employing four distinct cell types (three tumor cells and one non-tumor cell). The Examiner asserts that the subject matter of the claim is not adequately described in the specification, since a "plurality of distinct cell types" "would be broader in scope than the three recited tumor cells."

The CCPA, in *In re Rasmussen*, made the observation: "that a claim may be broader than the

specific embodiment disclosed in a specification is in itself of no moment". This decision is referred to in §2163.05 of the MPEP (page 2100-174, Rev. 1 Feb 2003), which states:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species....there may be situations where one species adequately supports a genus. See, e.g., *In re Rasmussen*, 650 F.2d 1212,1214, 211 USPQ 323, 326-7 (CCPA 1981) (disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim to "adheringly applying" because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered)...

In the present case, one skilled in the art reading the specification would understand that it was unimportant whether the claimed method, using distinct cell types, employed three, four, or any other number of distinct cell types. Nor would it be critical what specific cell types were employed. Such a person would understand that the applicants were in possession of a method employing a plurality of cell types, and not simply a method employing four cell types, or three tumor cell types.

III. Rejections under 35 U.S.C. §112, Second Paragraph

The Office Action states that claims 13-17, 21, 24-29 are rejected under 35 U.S.C. §112, second paragraph, "for reasons advanced in the last Office action". However, it then goes on to state that the "rejections under paragraph A-E have been overcome". Since these were all the rejections that were made under this section in the last Office action, to the applicants' understanding, it appears that no rejections under this section remain.

IV. Rejections under 35 U.S.C. §102(b)

Claims 13-15, 21-22, 24-25 and 27-29 were rejected under 35 U.S.C. §102(b) as being anticipated by Murphy *et al.*, *PNAS* **95**:1517, 1998. This rejection is respectfully traversed for the following reasons.

The standard for lack of novelty, that is, for anticipation, is one of strict identity. *Hybritech*

Inc. v. Monoclonal Antibodies, Inc., 802 F2d 1367, 231 USPQ 81, 90 (Fed. Cir. 1986); *In re Donohue*, 766 F2d 531, 226 USPQ 619, 621 (Fed. Cir. 1985). To anticipate a claim for a patent, a single prior source must contain all its essential elements.

A. The Invention

The applicant's invention, as embodied in independent claim 13, is directed to a method of identifying peptoids, in a library of different-sequence peptoids, which are effective in transfecting a cell with an oligonucleotide, the method comprising:

(i) contacting each peptoid in the library with an oligonucleotide, to form a plurality of peptoid-oligonucleotide mixtures,

(ii) contacting each said mixture with a cell;

(iii) screening each cell for transfection of the oligonucleotide, to identify transfected cells; and

(iv) identifying transfecting peptoids in mixtures contacted with transfected cells.

B. The Cited Art

Murphy *et al.* describe identification of cationic peptoids which are effective in the delivery of plasmid DNA (pCMV-km-LUC; see "Plasmids and Cell Lines" on page 1518). The pCMV-km-LUC plasmid is described in U.S. Patent No. 6,468,986, enclosed herewith, by the same authors. According to Example 5 of the '986 patent, the plasmid has over 4,000 basepairs. (See e.g. column 43, lines 19-29: "The plasmid used in these experiments, pCMVkmLUC, was constructed by inserting the luc+gene from pSP-luc+ ...into the expression vector pCMVkm2....The sequence of pCMVkm2 is depicted in SEQ ID NO:2", which has 4328 base pairs.)

This plasmid DNA would clearly not be considered an "oligonucleotide" as that term is known to those skilled in the art. A typical definition of the term "oligonucleotide" is "a short sequence of nucleotides" (ST Nicholl, *An Introduction to Genetic Engineering*, Cambridge University Press, 1994). The more generic term "oligomer" is defined as a "general term for a short polymer most commonly consisting of amino acids (oligopeptides), nucleic acids (oligonucleotides)..." in H Lodish *et al.*, *Molecular Biology* (Scientific American Books, Inc. 1998).

Even applying the standard that a claim term is to be given its broadest reasonable construction during prosecution, expanding the scope of the term "oligonucleotide" to include a 4328-base pair plasmid DNA would not be considered reasonable by one skilled in the art. Accordingly, the reference does not show the step of (i) "contacting each peptoid in the library with an oligonucleotide".

Because the reference does not disclose all of the elements set out above in claim 13 and its dependent claims, the claims cannot be anticipated by this reference under 35 U.S.C. §102(b). In view of this, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §102(b).

V. Rejections under 35 U.S.C. §103(a)

Claims 13-17 and 21-29 were rejected under 35 U.S.C. §103(a) as being unpatentable over Murphy *et al.*, above, in view of Fasbender *et al.* (U.S. Patent No. 5,935,936). The rejections are respectfully traversed in light of the following remarks.

A. The Invention

The invention of independent claim 13, as described above, is directed to a method of identifying peptoids, in a library of different-sequence peptoids, which are effective in transfecting a cell with an oligonucleotide. The method comprises:

(i) contacting each peptoid in the library with an oligonucleotide, to form a plurality of peptoid-oligonucleotide mixtures,

(ii) contacting each said mixture with a cell;

(iii) screening each cell for transfection of the oligonucleotide, to identify transfected cells; and

(iv) identifying transfecting peptoids in mixtures contacted with transfected cells.

B. The Cited Art

Murphy *et al.*, as noted above, describes identification of cationic peptoids which are effective in the delivery of plasmid DNA. The plasmid DNA exemplified, as noted above, has over 4,000 basepairs. There is no disclosure or suggestion of oligonucleotide delivery.

With regard to claims 23 and 26, the Examiner notes that "Murphy does not disclose the lipid steroid...attached to the peptoid". The Examiner cites Fasbender as allegedly providing the missing disclosure: "Fasbender *et al.* discloses...cationic amphiphiles containing steroid, as the commonly known DC-chol" (page 7 of Office Action).

However, the authors disclose the cationic amphiphiles, such as DC-chol, in the background discussion (see e.g. column 3, lines 6-9), and characterize these compounds as having "only modest activity" and providing uptake efficiencies which are "insufficient to support numerous therapeutic applications" (column 3, lines 27-35; emphasis added).

They address this insufficiency by employing, for transfection, a mixture of a cationic amphiphile, typically a conjugate of cholesterol with an aliphatic polyamine such as spermine (column 4, lines 65-67, and following), with a separate co-lipid, typically a phospholipid (column 4, lines 11-63).

Accordingly, the reference teaches away from the use of a steroid attached to a cationic moiety as a delivery vehicle, in the absence of a separate co-lipid.

Neither of the cited references, alone or in combination, provides any motivation to test peptoid compounds for delivery of oligonucleotides. The claims therefore cannot be found obvious over this combination of references.

C. The Examiner's Remarks

The Examiner stated that "one would have been motivated to use an oligonucleotide" by the teachings of Murphy *et al.* "since Murphy discloses that this long chain polynucleotide are subject to degradation on delivery to the target site". The applicants believe that this perceived problem would be more likely to motivate the skilled person to find ways of preventing this degradation of the long chain polynucleotides.

The Examiner next states that "One skilled in the art knows that these polynucleotides are normally condensed into its oligonucleotide to protect it from enzyme degradation". The applicants do not see the logic in this statement, since a polynucleotide which is "protected from enzyme degradation" would more likely be prevented from forming "oligonucleotides".

The Examiner then states that "Murphy discloses that the peptoids condenses the polynucleotide to a smaller size. In such condensation and degradation [sic], the DNA may have been converted to its smaller fragments...This would be at least suggestive of the claimed

oligonucleotides."

The Examiner seems to suggest that "degradation" is implied by the term "condensation". On the contrary, peptoids are repeatedly characterized in Murphy *et al.* as having the desired property of protecting DNA from degradation (e.g. Abstract; first and fourth paragraphs on page 1517).

Applicants also note that "condensing the polynucleotide to a smaller size" refers to condensing the DNA molecule to a smaller physical size, not to shorter lengths ("Condensation of DNA by cationic polymers...has been shown to protect supercoiled DNA from degradation", page 1519, column 1; "the most effective transfection reagent... condensed DNA into highly homogenous spherical particles whose diameters were around 50-60 nm"; page 1520, column 2).

Since a primary motivation in Murphy *et al.* is protection of long chain polynucleotides from degradation, any occurrence of "oligonucleotides" would be something to be avoided. The reference is therefore not "suggestive of oligonucleotides".

In view of the foregoing, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §103(a).

VI. Conclusion

In view of the foregoing, the applicant submits that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4403.

Respectfully submitted,

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